PATENT NO : 7,071,192 B1
APPLICATION NO. : 10/019,376
ISSUE DATE : 1,014,4,2006

SSUE DATE : July 4, 2006

INVENTOR(S) : Frans Eduard Janssens et al.

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title Page,

Item (57), ABSTRACT:

Line 19, delete "a position" and insert -- α position --.

Line 30, delete "-(CH₂)₅-"and insert -- -(CH₂)₈- --.

Line 33, delete "pyridazinyl, pyridazinyl;" and insert -- pyryzinyl, pyridazinyl; --.

Column 2.

Line 38, delete "=CH_C(=O)_NR5aR5b," and insert -- =CH-C(=O)-NR5aR5b, --.

Column 3,

Line 16, delete "-NR2 or" and insert -- -NR2-or --.

Line 37, delete "C1-6alkyloxy(-CH2-CH2-O)o-," and insert

-- C₁₋₆alkyloxy(-CH₂-CH₂-O)_n-, --.

Column 4,

Line 33, delete "C1-6alkyl-SO2-NR50," and insert -- C1-6alkyl-SO2-NR50-, --.

Line 34, delete "SO2-NR5c," and insert -- SO2-NR5c-, --.

Lines 34-35, delete "-C(=O)-NR5CR5d," and insert -- -C(=O)-NR5cR5d, --.

Line 35, delete "HO(CH2-CH2-O)n-," and insert -- HO(-CH2-CH2-O)n-, --.

 $\label{eq:ch2-ch2-one} Line~36,~delete~``C_{1-6}alkyloxy(-CH_2-CH_2-O)_n~-,"~and~insert~-~C_{1-6}alkyloxy(-CH_2-CH_2-O)_n-,$

. Line 37, delete "arylC₁₋₆alkyloxy(CH₂-CH₂-O)_n-" and insert

-- arylC₁₋₆alkyloxy(-CH₂-CH₂-O)_n- --.

Line 44, delete "C₃₋₇Cycloalkyl" and insert -- C₃₋₇cycloalkyl --.

Line 63, delete "C1_alkyloxy;" and insert -- C1_6alkyloxy; --.

Column 5,

Line 16, delete "C1-4alkyl" and insert -- C1-6alkyl --.

Line 23, delete "C1alkyl" and insert -- C1-6alkyl --.

Column 6,

Lines 66-67, after "and the like." insert new paragraph beginning with "The term "quaternary...".

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Column 7.

Line 23, delete "corn pounds" and insert -- compounds --.

Column 8,

Line 20, delete "arvl C1.6alkvl," and insert -- arvlC1.6alkvl, --.

Line 23. delete "C1.6 alkylcarbonylamino," and insert -- C1.6alkylcarbonylamino, --.

Line 23, after "C1.6 alkylcarbonylamino," insert -- C1.6 alkyl-SO2-NR50-, aryl-SO2-NR50-, C1. 6alkyloxycarbonyl, -C(=O)-NR5cR5d, --.

Line 23, delete "-CH2-CH2-O)n-," and insert -- HO(-CH2-CH2-O)n-, --.

Line 25 delete "arylC₁₋₆ alkyloxy(-CH₂-CH₂-O)_{ns}-" and insert -- arylC₁₋₆alkyloxy(-CH₂-CH₂-

O)_n- --.

Lines 25-26, delete "di (C1.6alkyl)amino" and insert -- di(C1.6alkyl)amino --.

Line 38, delete "C1-alkyl," and insert -- C1-6alkyl, --.

Line 47, delete "NR2," and insert -- -NR2-, --.

Line 55, delete "C1-6alkyloxy(-CH2-CH2)n-," and insert -- C1-6alkyloxy(-CH2-CH2-O)n-, --. Line 59, delete "(2-aminoethyl)₄-piperidinyl]" and insert -- (2-aminoethyl)-4-piperidinyl] --.

Line 62, delete "(2-amino-3-methylbutyl)4-piperidinyll" and insert -- (2-amino-3-methylbutyl)-4-piperidinyl] --.

Line 65, delete "(2-amino-3-methylbutyl)4-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-niperidinyll --.

Line 66, delete "-8-quinolinylmethyl]4-methyl" and insert -- -8-quinolinylmethyl]-4-methyl --.

Column 9,

Line 1, delete "(2-amino-3-methylbutyl)4-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyl] --.

Line 4, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyl] --.

Line 7, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyll --.

Line 9, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyll --.

Line 15, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyll --.

Line 18, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyl] --.

Line 21. delete "(2-aminoethyl),-piperidinyll4-methyl" and insert -- (2-aminoethyl)-4piperidinyl]-4-methyl --.

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Line 25, delete "(2-aminoethyl)₄-piperidinyl]-1-" and insert -- (2-aminoethyl)-4-piperidinyl]-1-

Line 28, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyl] --.

Line 31, delete "-2-methylpropyl]4-piperidinyl]" and insert -- -2-methylpropyl]-4-piperidinyl]

Line 34, delete "(2-aminoethyl),-piperidinyl]" and insert -- (2-aminoethyl)-4-piperidinyl] -- Line 37, delete "(2-amino-3-methylbutyl),-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyl] --

Line 40, delete "(2-aminoethyl)₄-piperidinyl]" and insert -- (2-aminoethyl)-4-piperidinyl] --. Line 49, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-

4-piperidinyl] --.

Line 51, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyl] --.

Line 54, delete "tetrahydro-5-quinoxalinyl)₄-methyl-" and insert -- tetrahydro-5-quinoxalinyl)-4-methyl- --.

Line 56, delete "(2-aminoethyl)₄-piperidinyl]" and insert -- (2-aminoethyl)-4-piperidinyl] --.
Line 59, delete "(2-amino-3-methylbutyl)₄-piperidinyll" and insert -- (2-amino-3-methylbutyl)-

Line 59, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyl] --Line 62, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-

4-piperidinyl] --.
Line 65, delete "(2-aminoethyl)₄-piperidinyl]" and insert -- (2-aminoethyl)-4-piperidinyl] --.
Line 66, delete "tetrahydro-5-quinoxalinyl)-methyl." and insert -- tetrahydro-5-quinoxalinyl)-

4-methyl- --. Column 10.

Line 1, delete "(2-aminoethyl)₄-piperidinyl]" and insert

-- (2-aminoethyl)-4-piperidinyl] --.

Line 2, delete "8-quinolinylmethyl]4-methyl" and insert -- 8-quinolinylmethyl]-4-methyl --, Line 4, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyl] --

Line 7, delete "(2-aminoethyl)4-piperidinyl]" and insert

-- (2-aminoethyl)-4-piperidinyl] --.

Line 10, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyl] --.

Line 14, delete "(2-amino-3-methylbutyl)₄-piperidinyl]" and insert -- (2-amino-3-methylbutyl)-4-piperidinyl] --.

Line 15, delete "tetrahydro-5-quinoxalinyl)₄-methyl-" and insert -- tetrahydro-5-quinoxalinyl)-4-methyl- --.

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Line 16, after "benzimidazol-2-amine;" insert new paragraph beginning "the prodrugs, the Novides, the....".

Line 17, delete "famines," and insert -- amines, --.

Line 64, delete "for example C] 4alkyloxycarbonyl," and insert -- for example C1-4alkyloxycarbonyl, --.

Column 12,

Line 28, after "and the like." insert new paragraph beginning "Compounds of formula...".

Column 14,

Line 38, delete "R\"-C_{1-c}alkyloxyC_{1-c}alkyl," and insert -- R\"-C_{1-c}alkyloxyC_{1-c}alkyl, --. Line 62, delete "H₂N-CH₂-CHOH-CH₂-Q_a', "and insert -- H₂N-CH₂-CHOH-CH₂-Q_a', --.

Column 15,

Line 57, delete "R" and insert -- R² --.
Line 58, delete "R²-NH-" and insert -- R^{2a}-NH---.

Column 16,

Line 63, delete "on R1 ranging" and insert -- on R1a ranging --.

Column 17,

Line 5, delete "R1a," and insert -- R1a, --.

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Lines 45-55, Compound (I-d-1), delete

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and insert --

Column 18,

Line 20, delete "(XVIII)" and insert -- (XVII) --. Line 46, delete "CH₂-C₁₋₃alkyl-NR," and insert -- CH₂-C₁₋₃alkyl-NR⁴, --.

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Lines 55-65, delete

$$= C - C_{1-3} a |ky| - NR^4$$

$$= N - 3 a^4$$

$$= A^2 + Q_6 N - H$$

(XIX)

and insert --

(XIX) (XX)

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Column 20, Lines 20-30, delete

$$Q \xrightarrow{\text{(O=)G_1}} A^{1} \xrightarrow{a^{1}} A^{2} \xrightarrow{\text{reduction}}$$

(XXII)

and insert --

$$R^1$$
 $O=O_{G_2}$
 $O=O_{G_2}$

Lines 50-51, delete "benzenecarboper-oxoic" and insert -- benzenecarboperoxoic --. Line 52, delete "3-chlorobenzenecarbo-peroxoic" and insert -- 3-chlorobenzenecarboperoxoic

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Column 21,

Line 28, delete "said R or" and insert -- said R^2 or --. Line 67, delete " Z^1 ," and insert -- Z_1 , --.

Column 22,

Lines 58 -67, delete

$$Z_{1a} - Q_1$$
 Q_1
 Q_1
 Q_2
 Q_3
 Q_4
 Q_4
 Q_4
 Q_4
 Q_5
 Q

(I-a-2)

and insert --

$$C_{1a} - Q_1 - Q$$

(I-h-2)

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Column 23,

Line 39, delete "wherein R₁" and insert -- wherein R¹ --. Line 41, delete "HO-R¹-," and insert -- HO-R¹', --.

Line 46, delete "Z2-O-R1-." and insert -- Z2-O-R1'. --.

Column 24,

Lines 28-38, delete

(XXVI)

(I-I-2)

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and insert --

(I-I-2)

Column 25.

Line 30, delete "formula (E)" and insert -- formula (III) --.

Line 45, delete "formula (XXVI)," and insert -- formula (XXVII), --.

Line 50, delete "of R1-" and insert -- of R1' --.

Column 26,

Line 19, delete "Gi" and insert -- G --.

Line 20, delete "formula (ff-a)" and insert -- formula (III-a) --.

Line 43, delete "a-suitable" and insert -- a suitable --.

Column 27,

Line 11, delete "R₁-CH₂-OH," and insert -- R¹-CH₂-OH, --.

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Column 28, Lines 52-65, delete

XCIV

and insert --

XCIV _

Column 29,

Line 2, delete "formula (XXXII-a) or (XXXI-b)," and insert -- formula (XXXIII-a) or (XXXIII-b), --.

Line 5, delete "formula (E)" and insert -- formula (III) --.

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Column 31,

Line 48, delete "R₅₀R_{5b}N-R¹," and insert -- R^{5a}R^{5b}N-R¹, --,

Column 32,

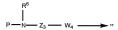
Line 18, delete "R5aR5>N-C(=O)-R1'," and insert -- R5aR5bN-C(=O)-R1', --.

Line 54, delete "formula (TV)" and insert -- formula (IV) --.

Line 61, delete "formula (XU)," and insert -- formula (XLI), --.

Column 33,

Lines 5-10, delete



and insert --

Line 25, delete "hydroxyC1.alkyl," and insert -- hydroxyC1.6alkyl, --.

Column 34,

Line 28, delete "formula (XXXII-a)" and insert -- formula (XXXIII-a) --.

Line 34, delete "formula (XXXII-a) or (XXXII-b)," and insert -- formula (XXXIII-a) or (XXXIII-b), --.

Line 38, delete "formula (XXXII-a-1)" and insert -- formula (XXXIII-a-1) --.

Column 35.

Line 13, delete "or (XLVI-b)" and insert -- or (XLVII-b) --.

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Column 36,

Lines 25-32, delete

$$H_2N$$
 A^2
 A^3
 A^3

(XLVIII-b)

and insert --

$$H_2N$$
 A_2
 A_3
 A_4
 A_3
 A_4
 A_4

Column 37,

(XLVIII-a)

Line 53, delete "formula (m)" and insert -- formula (III) --.

Column 38,

Line 45, delete "inter-mediates" and insert -- intermediates --.

Line 48, delete "formula (LVII)" and insert -- formula (LVIII) --.

Line 48, delete "Nd N-diisopropylamine" and insert -- N,N-diisopropylamine --.

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Column 39,

Line 6, delete "Z-O-G₁," and insert -- Z₄-O-G₁, --.

Line 63, delete "formula (Iv-g)," and insert -- formula (IV-g), --.

Column 40,

Line 64, delete "formula (XXXII-a)" and insert -- formula (XXXIII-a) --.

Column 41.

Line 29, delete "formula (LX)" and insert -- formula (LXIX) --.

Line 63, delete "formula (XXXII-a)" and insert -- formula (XXXIII-a) --.

Column 43,

Line 14, delete "formula (LXXI)" and insert -- formula (LXXII) --. Line 40, delete "Of" and insert -- of --.

Column 44.

Line 19, delete "formula (LXX-a)," and insert -- formula (LXXI-a), --. Lines48-49, delete "formula (LXXI-b)," and insert -- formula (LXXI-b), --.

Line 50, delete "formula (I)" and insert -- formula IX --.

Column 46,

Line 62, delete "Of" and insert -- of --.

Line 63, delete "Q3," and insert -- Q3', --.

Line 64, delete "arid said inter-mediates" and insert -- and said intermediates --.

Column 47.

Line 22, delete "formula (LXXX)" and insert -- formula (LXXXI) --.

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Lines 38-45, delete

$$\begin{array}{c|c} S \\ \hline \\ O_{2} \\ \hline \\ O_{2N} \\ \end{array}$$

and insert --

$$\begin{bmatrix} S \\ Q_3 \\ NH \end{bmatrix}$$

$$H_2N$$

$$A^3$$

$$A^3$$

$$A^3$$

$$A^3$$

$$A^3$$

$$A^3$$

Column 48,

- Line 2, delete "Of" and insert -- of --.
- Line 2, delete "Comprises" and insert -- comprises --.
- Line 5, delete "formula (LXXV)," and insert -- formula (LXXXV), --.

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Column 49,

Line 25, delete "Q4," and insert -- Q4--.

Line 28. delete "inter-mediate" and insert -- intermediate --.

Column 50.

Line 41, delete "anti viral" and insert -- antiviral --.

Line 53, delete "38, 3142)." and insert -- 38, 31-42). --.

Column 53.

Line 45, delete "(NH₄OH" and insert -- /NH₄OH --.

Line 58, delete "=extracted" and insert -- extracted --.

Column 54,

Line 9, delete "(10 g)" and insert -- (100g) --.

Line 48, delete "yl]amino] 1" and insert -- yl]amino]-1 --.

Column 55.

Line 5, delete "a 34 bar" and insert -- a 3-4 bar --.

Line 9, delete "NH4 OH" and insert -- NH4OH --.

Line 37, delete "(O)-5,6,7,8-" and insert -- (±)-5,6,7,8- --.

Line 59, delete "N-2,6-dimetyl-2,3-pyridinediamine" and insert -- N-2,6-dimethyl-2,3-pyridinediamine --.

Column 56.

Line 18, "(trifluoromethyl)1H" and insert -- (trifluoromethyl)-1H --.

Line 49, delete "2-yl]amino])1 piperidinecarboxylate" and insert -- 2-yl]amino]-1-

piperidinecarboxylate --.

Line 65, delete "elm)," and insert -- um), --.

Column 57,

Line 34, delete "4-[[1-(8-quinolinylmethyl): 1H-imidazo[4," and insert -- 4-[[1-(8-quinolinylmethyl)-1H-imidazo[4, --.

Column 58,

Line 55, delete "portion wise," and insert -- portionwise, --.

Line 59, delete " $(\pm)_4$ -[[1" and insert -- (\pm) -4-[[1- --.

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Column 59,

Line 11, after "(interm." insert -- 36). --. Line 67, delete "Nail" and insert -- NaH --.

Column 60,

Line 2, delete "stir-ring" and insert -- stirring --.

Line 26, delete "(±)-N-[1" and insert -- (±)-N-[1- --.

Line 31, delete "(60 ma)." and insert -- (60 ml). --.

Line 33, delete "MgSO₄)," and insert -- (MgSO₄), --.

Line 43, delete "yl]amino]1-piperidinyl]-3-methyl-2-butanone" and insert -- yl]amino]-1-piperidinyl]-3-methyl-2-butanone --.

Column 61,

Line 14, delete "CH2Cl2/CH3OH/N OH" and insert -- CH2Cl2/CH3OH/NH4OH --.

Lines 14-15, delete "1540 em)." and insert -- 15-40 μm). --.

Line 18, delete "(4-quinolinylmethy)1H-benzimidazol-2-yl]" and insert -- (4-quinolinylmethy)-1H-benzimidazol-2-yl] --

Column 62,

Line 29, delete "CH2Cl2/H3OH" and insert -- CH2Cl2/CH3OH --.

Line 30, delete "35-70 cm)." and insert -- 35-70 μm). --.

Column 64,

Line 19, delete "NH4OH." and insert -- NH4OH --.

Column 68.

Line 61, delete "stir-red" and insert -- stirred --.

Column 69,

Line 12, delete "amino]-1'-piperidinyl]" and insert -- amino]-1-piperidinyl] --.

Line 19, delete "N-[1-(2-aminoethyl)4-" and insert -- N-[1-(2-aminoethyl)4---.

Line 29, delete "1540 em)." and insert -- 15-40 μm). --.

Lines 34-35, delete "piperidinyl]4-methyl-1-" and insert -- piperidinyl]-4-methyl-1- --.

Line 44, delete "CH₂/Cl₂/CH₃OH NH₄OH" and insert -- CH₂/Cl₂/CH₃OH/NH₄OH --.

Line 53, delete "15-40 em)," and insert -- 15-40 µm), --.

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Column 70,

Line 14, delete "aminoethyl)4-piperidinyl]" and insert -- aminoethyl)-4-piperidinyl] --.

Column 7

Line 65, delete "(0.0021-O-mol)" and insert -- (0.00218 mol) --.

Column 7

Lines 14-15, delete "methylbutyl)4-piperidinyl]" and insert -- methylbutyl)-4-piperidinyl] --.

Column 73.

Lines 23-24, delete "15-40 em)." and insert -- 15-40 μm). --.

Column 96.

Line 62, delete "activity-or" and insert -- activity or --.
Line 64, delete "anti viral" and insert -- antiviral --.

Column 97.

Line 23, delete "MT" and insert -- MTT --.

Column 98,

Line 4, delete "CH₆alkyl," and insert -- C_{1.6}alkyl, --. Line 5, delete "CH₆alkyloxy," and insert -- C_{1.6}alkyloxy, --. Lines-29-34, delete

$$R_2$$
 N
 X^1
 $(CH_2)_t$
 $(b-3)$

.

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and insert

$$R^2 - N X^1 - (CH_2)_1$$
(b-3)

Line 60, delete " $-NR^2$ or" and insert -- $-NR^2$ or --. Line 64, delete " $CH(NR_{5a}R_{5b})$," and insert -- $CH(NR^{5a}R^{5b})$, --.

Column 99,

Line 16, delete "(-CH₂CH₂-O)_n-," and insert -- (-CH₂-CH₂-O)_n-, --. Lines 24-25, delete "imidazo[4,5b]pyridinyl," and insert -- imidazo[4,5-b]pyridinyl, --.

Column 100.

Line 22, delete "(-CH2CH2-O)n-" and insert -- (-CH2-CH2-O)n- --.

Line 34, delete "N(R 6)2" and insert -- N(R6)2 --.

Line 43, delete "CH6alkyl;" and insert -- C1-6alkyl; --.

Line 45, delete "-(CH2)n-" and insert -- -(CH2)s- --.

Line 46, delete "CH4alkyl," and insert -- C14alkyl, --.

Line 47, delete "CH6alkylcarbonyl" and insert -- C1-6alkylcarbonyl --.

Line 49, delete "CH6alkyl," and insert -- C16alkyl, --.

Line 51, delete "CH6alkyloxy;" and insert -- C16alkyloxy; --.

Column 101,

Line 29, after "isoquinolinylmethyl)" insert -- - --.

Column 102.

Line 4, delete "claims 1 and 3 to 6." and insert -- claims 1 and 2 to 5. --. Line 27, delete "Q1" and insert -- Q1 --.

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Column 103,

Line 52, delete "H-Q," and insert -- H-Q1 --.

Column 107,

Line 35, delete "H2N-CH2-CHOH-CH2-Q4" and insert -- H2N-CH2-CHOH-CH2-Q4 ---

Column 108,

Line 59, delete "N(R6)2" and insert -- N(R6)2 --.

Column 109,

Lines 26-53, delete

$$P = Q$$
 $A = R$
 $A =$

and insert

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Column 110,

Line 16, delete "H-Q," and insert -- H-Q₁ --.

Line 18, delete " $R^{1a}(A-O-H)_w$," and insert -- $R^{1a}-(A-O-H)_w$, --.

Lines 18-19, delete " $R_{1a'}$ (A-O-H)₃" and insert -- $R^{1a''}$ (A-O-H)₃ -- Line 51, delete " R^1 , G, $-a^1 = a^2 - a^3 = a^4$ -, "and insert -- R^1 , G, $-a^1 = a^2 - a^3 = a^4$ -, ...

Column 111,

Line 33, delete "HO-G1" and insert -- HO-G1 --.

Line 35, delete "HO(CH2CH2O-)n;" and insert -- HO-(CH2CH2O-)n; --.

Column 112.

Line 15, delete "-a1=a 2-a3=a4-" and insert -- -a1=a2-a3=a4---.

Line 23, delete "(I')," and insert -- (I), --.

Line 29, delete "(I')," and insert -- (I), --.

Line 36, delete "(I')," and insert -- (I), --.

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